REMARKS

Overview

Applicants have reviewed and considered the Office Action dated December 15, 2004 and the references cited therewith. Applicants note that claims 4-20 and 37-43 are pending in this application. Claims 13, 20, 42 and 43 have been amended. Claims 44-45 have been added. Support for these amendments can be found in the published Specification, at paragraphs 91, 98, 160-162, and 216-218.

Claim Rejections - 35 U.S.C. § 112

Claims 13, 20, 42 and 43 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Examiner states that the recitation of the phrase "of the pharmaceutically acceptable carrier of sodium chloride" in the last line of claims 13 and 42 renders the claim indefinite because it is unclear whether the sodium chloride is the carrier or the carrier is designed to carry the sodium chloride.

Applicants thank the Examiner for the suggested language which they have adopted so that claim 13 now recites "The pharmaceutical composition of claim 12 comprising an antimicrobial compound in an amount of from 0.5% by weight to 0.8% by weight and wherein the pharmaceutically acceptable carrier comprises sodium chloride in an amount of from 0.5% by weight to 1.0% by weight of the pharmaceutical composition." Accordingly, claim 42 has been amended so that it now recites "The pharmaceutical composition of claim 7 comprising an antimicrobial compound in an amount of from 0.5% by weight to 0.8% by weight and wherein

the pharmaceutically acceptable carrier comprises sodium chloride in an amount of from 0.5% by weight to 1.0% by weight of the pharmaceutical composition."

The Examiner states that claims 20 and 43 recites the limitation "the infection" in line 2 of the claims. The Examiner states there is insufficient antecedent basis for this limitation in the claim because it depends from claim 15 and 12 respectively and there is no "infection" recited in the claims from which these claims depend. Accordingly, Applicants have amended claim 15 from which claim 20 depends so that claim 15 recites "A pharmaceutical composition for treating an infection in an animal comprising:". Claim 43 has been amended so that it now depends from claim 5. Applicants believe they have alleviated Examiner's concern and request that this rejection be withdrawn and reconsidered.

Claim Rejections - 35 U.S.C. § 103

A. Claims 4-6, 8-20 and 43

The Examiner states that claims 4-6, 8-20 and 43 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ropapharm B.V., EP 0904780A1 in view of Avery's Drug Treatment, 4th Edition, Chapter 31, pp. 1455-1509.

The Examiner states that Ropapharm teaches a pharmaceutical composition in the form of a solution comprising Carvacrol and/or Thymol, water, Emulgator 686 and polysorbate as being suitable for the treatment of diseases caused by Salmonella spp., Pasteurella spp., E. coli, Vibrio coli, etc. (page 2, col. 1, line 55 to col. 2, line 5).

The Examiner states that Avery teaches that the dosage regimens recommended by the manufacturers of Antimicrobial drugs are purely arbitrary. The Examiner states that the secondary reference gives guides for determining dosage amounts, but say that the values will

depend on the health, age, and pharmacokinetic characteristics of the patient (page 1489, col. 1, 4). The Examiner states that while the references are silent regarding the specific percentages by weight of thymol and carvacrol as claimed instantly, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical.

Applicants respectfully disagree. An invention can be obvious even though the suggestion to combine prior art teachings is not found in a specific reference. *In re Oetiker*, 24 USPQ2d 1443 (Fed. Cir. 1992). At the same time, however, although it is not necessary that the cited references or prior art specifically suggest making the combination, there must be some teaching somewhere which provides the suggestion or motivation to combine prior art teachings and applies that combination to solve the same or similar problem which the claimed invention addresses. One of ordinary skill in the art will be presumed to know of any such teaching. (See, e.g., *In re Nilssen*, 851 F.2d 1401, 1403, 7 USPQ2d 1500, 1502 (Fed. Cir. 1988) and *In re Wood*, 599 F.2d 1032, 1037, 202 USPQ 171, 174 (CCPA 1979)).

Applicants respectfully submit that the Office Action did not make out a *prima facie* case of obviousness for the following reasons: even if combined, the cited references fail to teach or suggest all of the elements of applicants' claimed invention. The references when combined must teach or suggest all the claim elements. M.P.E.P. § 2142.

Claim 5 recites: A pharmaceutical composition for treating an infection in an animal comprising: (a) at least one antimicrobial compound comprising an organic phenolic compound reacted with at least one Group I hydroxide base; and (b) a pharmaceutically acceptable carrier for parenteral administration.

Applicants teach in the Published Specification at paragraph 55, that "the term "reacting" refers to a process in which the organic phenolic compound is chemically modified (as compared to the formation of a solution). In the formation of an antimicrobial compound with a Group I base, the reaction of the organic phenolic compound involves the deprotonation of the alcohol moiety to form an aryl oxide anion which then associates with the Group I cation in solution."

In contrast, the Ropapharm patent '780 describes the preparation of thymol and/or carvacrol in a water-soluble solution. Both Avery's Drug Treatment and '780 are silent as to reacting an organic phenolic compound reacted with at least one Group I hydroxide base. The references do not teach or suggest at least one antimicrobial compound comprising an organic phenolic compound reacted with at least one Group I hydroxide base, as recited in claim 5. Furthermore, even if a salt was added to the water-soluble solution described in the '780 patent, there is no teaching that they appreciated or recognized that "[t]he association of the organic phenolic compound with sodium or potassium appears to increase the rate of pathogen destruction" as taught by the Applicants. Published Specification, at paragraph 51. Thus, claim 5 is not obvious. Dependent claims 4, 6, 8-12, 19 and 43 depending from independent claim 5 are patentable over the combination of '780 and Avery for the reasons argued above plus the elements in the claim. Likewise, independent claim 14 is not obvious for the reasons argued above plus the elements in the claim.

Applicants respectfully submit that the Office Action did not make out a *prima facie* case of obviousness for the following reasons: the '780 patent teaches away from applicants' claimed invention. The '780 patent describes preferring active compounds in an organic state. For example, at Col. 2, lines 26-35, the '780 patent teaches that "[a]lthough above active compounds may have a synthetic origin, preferably the active compounds are applied in the form of an oil

extracted from any of the plants, selected from *Origanum vulgaris, Thymus vulgaris, Metha piperita, Thymus serpilum, Saturea hortensis, Saturea montana, Saturea subricata, Carum corticum, Thymus zugus, Ocimum gratismum, Moranda pungtata, Mosla japanoica,* and *Salva officinalis*. Avery's Drug Treatment does not describe reacting active compounds with a Group I hydroxide base.

The references teach away from the claimed combination because Applicants teach the synthesis of a base reacted antimicrobial compound from an organic phenolic compound, rather than using the active organic compound in its organic form. Published Specification, at paragraphs 57-62. Therefore, the '780 patent teaches away because a person of ordinary skill, upon reading the '780 patent, would be led in a direction divergent from the path the applicant took – reacting an organic phenolic compound with a Group I base to form a base reacted antimicrobial compound. *In re Gurley*, 27 F.3d 551, 31 USPQ 2d 1130, 1131 (Fed. Cir. 1994); *United States v. Adams*, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966); *In re Sponnoble*, 405 F.2d 578, 587, 160 USPQ 237, 244 (C.C.P.A. 1969); *In re Caldwell*, 319 F.2d 254, 256, 138 USPQ 243, 245 (C.C.P.A. 1963).

Furthermore, there is no teaching in either the '780 patent or Avery's Drug Treatment that levels of isopropyl-o-cresol and isopropyl cresol claimed by Applicants are effective in treating mastitis in a cow (Example 14a) or tendon inflammation in horses (Example 27). Thus, the claimed invention is not obvious. Therefore, Applicants respectfully request that the rejection to claims 4-6, 8-20 and 43 under 35 U.S.C. §103 be withdrawn and reconsidered.

B. Claims 4-9, 12-20 and 37-43

The Examiner states claims 4-9, 12-20 and 37-43 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ropapharm B.V. EP0904780A1 and further in view of Remington's Pharmaceutical Sciences, 15th Edition, 1975, pp. 1405-1412.

The Examiner states that Ropapharm teaches a pharmaceutical composition in the form of a solution comprising Carvacrol and Thymol, water, Emulgator 686 and polysorbate. The Examiner states that the reference teaches that the pharmaceutical compositions as being suitable for the treatment of diseases caused by Salmonella spp., Pasteurella spp., E. coli, Vibrio coli, etc. The Examiner states that the reference teaches the active ingredient in the form of thymol and/or carvacrol is present in an amount of from 1 to 10% by weight based on the total weight of the formulation for treatment of poultry, including turkeys, as in instant claim 19 and the use as an injectable composition comprising both thymol and carvacrol in amounts which overlap those claimed in instant claims 8-9 and 12, for the treatment of diseases caused by infections of instant claim 20.

The Examiner states that the primary reference lacks the sodium chloride of instant claims 13 and 42. The Examiner states that Remington teaches that knowledge of colligative properties of solutions is essential for one to understand fully the principles involved in rendering intravenous solutions isotonic with blood serum. The Examiner states that to produce less shock and less irritation than those which are hypotonic or hypertonic, and present-day practice recognizes the desirability of making the necessary adjustment whenever possible. The Examiner states that finally the secondary reference teaches that the usual practice is to add water with sodium chloride or dextrose to adjust hypotonic intravenous solutions to isotonicity.

Applicants respectfully disagree. Applicants respectfully submit that the Office Action did not make out a *prima facie* case of obviousness for the following reasons: even if combined, the cited references fail to teach or suggest all of the elements of applicants' claimed invention and the '780 patent teaches away from applicants' claimed invention. The references when combined must teach or suggest all the claim elements. M.P.E.P. § 2142.

Claim 5 recites: A pharmaceutical composition for treating an infection in an animal comprising: (a) at least one antimicrobial compound comprising an organic phenolic compound reacted with at least one Group I hydroxide base; and (b) a pharmaceutically acceptable carrier for parenteral administration.

Applicants teach in the Published Specification at paragraph 55, that "the term "reacting" refers to a process in which the organic phenolic compound is chemically modified (as compared to the formation of a solution). In the formation of an antimicrobial compound with a Group I base, the reaction of the organic phenolic compound involves the deprotonation of the alcohol moiety to form an aryl oxide anion which then associates with the Group I cation in solution."

In contrast, the Ropapharm patent '780 describes the preparation of thymol and/or carvacrol in a water-soluble solution. Both Remington's Pharmaceutical Sciences and '780 are silent as to reacting an organic phenolic compound reacted with at least one Group I hydroxide base. The references do not teach or suggest at least one antimicrobial compound comprising an organic phenolic compound reacted with at least one Group I hydroxide base, as recited in claim 5. Furthermore, even if a salt was added to the water-soluble solution described in the '780 patent, there is no teaching that they appreciated or recognized that "[t]he association of the organic phenolic compound with sodium or potassium appears to increase the rate of pathogen destruction" as taught by the Applicants. Published Specification, at paragraph 51. Thus, claim

5 is not obvious. Dependent claims 4, 6, 8-12, 19 and 43 depending from independent claim 5 are patentable over the combination of '780 and Remington's Pharmaceutical Sciences for the reasons argued above plus the elements in the claim. Likewise, independent claim 14 is not obvious for the reasons argued above plus the elements in the claim.

Applicants respectfully submit that the Office Action did not make out a *prima facie* case of obviousness for the following reasons: the '780 patent teaches away from applicants' claimed invention. The '780 patent describes preferring active compounds in an organic state. For example, at Col. 2, lines 26-35, the '780 patent teaches that "[a]lthough above active compounds may have a synthetic origin, preferably the active compounds are applied in the form of an oil extracted from any of the plants, selected from Origanum vulgaris, Thymus vulgaris, Metha piperita, Thymus serpilum, Saturea hortensis, Saturea montana, Saturea subricata, Carum corticum, Thymus zugus, Ocimum gratismum, Moranda pungtata, Mosla japanoica, and Salva officinalis. Remington's Pharmaceutical Sciences does not describe reacting active compounds with a Group I hydroxide base.

The references teach away from the claimed combination because Applicants teach the synthesis of a base reacted antimicrobial compound from an organic phenolic compound, rather than using the active organic compound in its organic form. Published Specification, at paragraphs 57-62. Therefore, the '780 patent teaches away because a person of ordinary skill, upon reading the '780 patent, would be led in a direction divergent from the path the applicants took – reacting an organic phenolic compound with a Group I base to form a base reacted antimicrobial compound. *In re Gurley*, 27 F.3d 551, 31 USPQ 2d 1130, 1131 (Fed. Cir. 1994); *United States v. Adams*, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966); *In re Sponnoble*, 405 F.2d

578, 587, 160 USPQ 237, 244 (C.C.P.A. 1969); *In re Caldwell*, 319 F.2d 254, 256, 138 USPQ 243, 245 (C.C.P.A. 1963).

Furthermore, there is no teaching in either the '780 patent or Remington's Pharmaceutical Sciences that levels of isopropyl-o-cresol and isopropyl cresol claimed by Applicants are effective in treating mastitis in a cow (Example 14a) or tendon inflammation in horses (Example 27). Thus, the claimed invention is not obvious. Therefore, Applicants respectfully request that the rejection to claims 4-9, 12-20 and 37-43 under 35 U.S.C. §103 be withdrawn and reconsidered.

C. Claims 10-11

The Examiner states claims 10-11 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ropapharm B.V., EP0904780A1 and further in view of Remington's Pharmaceutical Sciences, 15th Edition, 1975, pp. 1405-1412 as applied to claims 4-9, 12-20 and 37-43 above, taken together with The Merck Index, An Encyclopedia of Chemicals, Drugs, and Biologicals, 12th Edition, 1996, p. 9539, and common knowledge in the art.

The Examiner states that it would have been obvious to one having ordinary skill in the art at the time the invention was made to have modified the solution comprising Carvacrol and/or Thymol, water, Emulgator 686 and polysorbate, which is adjusted for isotonicity using either sodium chloride or dextrose, by adding olive oil as suggested by Merck, or by using a cheaper, easily obtained vegetable oil, because of the reasonable expectation of obtaining an injectable pharmaceutical composition, comprising a readily available pharmaceutically acceptable carrier, which has the desirable property of solubilizing thymol.

Applicants respectfully disagree. Applicants respectfully submit that the Office Action did not make out a *prima facie* case of obviousness for the following reasons: even if combined,

the cited references fail to teach or suggest all of the elements of applicants' claimed invention and the '780 patent teaches away from applicants' claimed invention. The references when combined must teach or suggest all the claim elements. M.P.E.P. § 2142.

Claim 10 recites "[t]he pharmaceutical composition of claim 5 comprising from 3.5% by weight of the pharmaceutical composition to 10% by weight of the pharmaceutical composition of antimicrobial compound, wherein the pharmaceutically acceptable carrier comprises a vegetable oil." Claim 5 recites "A pharmaceutical composition for treating an infection in an animal comprising: (a) at least one antimicrobial compound comprising an organic phenolic compound reacted with at least one Group I hydroxide base; and (b) a pharmaceutically acceptable carrier for parenteral administration."

Applicants teach in the Published Specification at paragraph 55, that "the term 'reacting' refers to a process in which the organic phenolic compound is chemically modified (as compared to the formation of a solution). In the formation of an antimicrobial compound with a Group I base, the reaction of the organic phenolic compound involves the deprotonation of the alcohol moiety to form an aryl oxide anion which then associates with the Group I cation in solution."

In contrast, the Ropapharm patent '780 describes the preparation of thymol and/or carvacrol in a water-soluble solution. Both Remington's Pharmaceutical Sciences and '780 are silent as to reacting an organic phenolic compound reacted with at least one Group I hydroxide base. The references do not teach or suggest at least one antimicrobial compound comprising an organic phenolic compound reacted with at least one Group I hydroxide base, as recited in claim 5. Furthermore, even if a salt was added to the water-soluble solution described in the '780 patent, there is no teaching that they appreciated or recognized that "[t]he association of the organic phenolic compound with sodium or potassium appears to increase the rate of pathogen

destruction" as taught by the Applicants. Published Specification, at paragraph 51. Thus, claim 5 is not obvious. Dependent claims 10-11 depending from independent claim 5 are patentable over the combination of '780 and Remington's Pharmaceutical Sciences for the reasons argued above plus the elements in the claim.

Applicants respectfully submit that the Office Action did not make out a *prima facie* case of obviousness for the following reasons: the '780 patent teaches away from applicants' claimed invention. The '780 patent describes preferring active compounds in an organic state. For example, at Col. 2, lines 26-35, the '780 patent teaches that "[a]lthough above active compounds may have a synthetic origin, preferably the active compounds are applied in the form of an oil extracted from any of the plants, selected from *Origanum vulgaris, Thymus vulgaris, Metha piperita, Thymus serpilum, Saturea hortensis, Saturea montana, Saturea subricata, Carum corticum, Thymus zugus, Ocimum gratismum, Moranda pungtata, Mosla japanoica*, and *Salva officinalis*. Remington's Pharmaceutical Sciences does not describe reacting active compounds with a Group I hydroxide base.

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578, 587, 160 USPQ 237, 244 (C.C.P.A. 1969); *In re Caldwell*, 319 F.2d 254, 256, 138 USPQ 243, 245 (C.C.P.A. 1963).

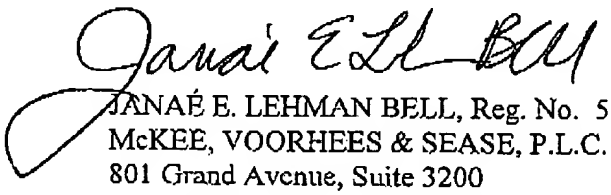
Furthermore, there is no teaching in either the '780 patent or Remington's Pharmaceutical Sciences that levels of isopropyl-o-cresol and isopropyl cresol claimed by Applicants are effective in treating mastitis in a cow (Example 14a), or tendon inflammation in horses (Example 27). Applicants remind Examiner that the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP § 2143. Thus, the claimed invention is not obvious. Therefore, Applicants respectfully request that the rejection to claims 10-11 under 35 U.S.C. §103 be withdrawn and reconsidered.

Conclusion

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,



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